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NEWS 6 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 7 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 8 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 9 MAR 22 EMBASE is now updated on a daily basis
NEWS 10 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 11 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC
thesaurus added in PCTFULL
NEWS 12 APR 04 STN AnaVist \$500 visualization usage credit offered
NEWS 13 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 14 APR 12 Improved structure highlighting in FQHIT and QHIT display
in MARPAT
NEWS 15 APR 12 Derwent World Patents Index to be reloaded and enhanced during
second quarter; strategies may be affected
NEWS 16 MAY 10 CA/CAPLUS enhanced with 1900-1906 U.S. patent records
NEWS 17 MAY 11 KOREAPAT updates resume
NEWS 18 MAY 19 Derwent World Patents Index to be reloaded and enhanced

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
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FILE COVERS 1907 - 25 May 2006 VOL 144 ISS 22

FILE LAST UPDATED: 24 May 2006 (20060524/ED)

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=> smallpox

L1 862 SMALLPOX

=> peptide (w) 165

349663 PEPTIDE

256201 PEPTIDES

447918 PEPTIDE

(PEPTIDE OR PEPTIDES)

58221 165

L2 4 PEPTIDE (W) 165

=> L1 and L2

L3 0 L1 AND L2

=> (HLA-A 0201)

32622 HLA

66 HLAS

32638 HLA

(HLA OR HLAS)

19779235 A

1695 0201

L4 660 (HLA-A 0201)

(HLA(W)A(W)0201)

=> L1 and L4

L5 8 L1 AND L4

=> D L2 IBIB ABS 1-4

L2 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:648407 CAPLUS
DOCUMENT NUMBER: 141:169001
TITLE: Identification of gene sequences and proteins involved
in vaccinia virus dominant T cell epitopes and use for
vaccination
INVENTOR(S): Terajima, Masanori; Cruz, John; Ennis, Francis A.
PATENT ASSIGNEE(S): University of Massachusetts Medical Center, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067032	A2	20040812	WO 2004-US2141	20040126
WO 2004067032	A3	20041125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
US 2005129703	A1	20050616	US 2004-764985	20040126
EP 1624890	A2	20060215	EP 2004-705315	20040126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:		US 2003-442846P	P	20030124
		WO 2004-US2141	W	20040126

AB The present invention relates to the identification of gene sequences and proteins involved in vaccinia virus dominant T cell epitopes. Two vaccinia virus CD8+ T cell epitopes restricted by the most common human MHC class I allele, HLA-A0201 have been identified. Both epitopes are highly conserved in vaccinia and variola viruses. The induction of the T cell responses following primary vaccination is demonstrated by the kinetics of epitope specific CD8+ T cells in 3 HLA-A0201 individuals. This information will be useful for the design and analyses of the immunogenicity of exptl. vaccinia vaccines, and for basic studies of human T cell memory.

L2 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:4546Q2 CAPLUS
DOCUMENT NUMBER: 135:266912
TITLE: Caveolin-1 peptide exerts cardioprotective effects in myocardial ischemia-reperfusion via nitric oxide mechanism
AUTHOR(S): Young, Lindon H.; Ikeda, Yasuhiko; Lefer, Allan M.
CORPORATE SOURCE: Department of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE: American Journal of Physiology (2001), 280(6, Pt. 2), H2489-H2495
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Caveolin-1 is a protein constituent of cell membranes. The caveolin-1 scaffolding region (residues 82-101) is a known inhibitor of protein kinase C. Inhibition of protein kinase C results in maintained nitric oxide (NO) release from the endothelium, which attenuates cardiac dysfunction after ischemia-reperfusion (I/R). Therefore, we hypothesized that the caveolin-1 scaffolding region of the mol., termed caveolin-1 peptide, might attenuate postischemia polymorphonuclear neutrophil (PMN)-induced cardiac dysfunction. We examined the effects of caveolin-1 peptide in isolated ischemic (20 min) and reperfused (45 min) rat hearts reperfused with PMNs. Caveolin-1 **peptide** (165 or 330 µg) given i.v. 1 h before I/R significantly attenuated postischemic

PMN-induced cardiac dysfunction, as exemplified by left ventricular developed pressure (LVDP) ($P < 0.01$) and the maximal rate of developed pressure ($+dP/dt_{max}$) ($P < 0.01$), compared with I/R hearts obtained from rats given 0.9% NaCl. In addition, caveolin-1 peptide significantly reduced cardiac PMN infiltration from 195 ± 5 PMNs/mm² in untreated hearts to 103 ± 5 and 60 ± 5 PMNs/mm² in hearts from 165 and 330 μ g caveolin-1 peptide-treated rats, resp. ($P < 0.01$). PMN adherence to the rat coronary vasculature was also significantly reduced in rats given either 165 or 330 μ g caveolin-1 peptide compared with rats given 0.9% NaCl ($P < 0.01$). Moreover, caveolin-1 peptide-treated rat aortas exhibited a 2.2-fold greater basal release of NO than vehicle-treated aortas ($P < 0.01$), and this was inhibited by NG-nitro-L-arginine Me ester. These results provide evidence that caveolin-1 peptide significantly attenuated PMN-induced post-I/R cardiac contractile dysfunction in the isolated perfused rat heart, probably via enhanced release of endothelium-derived NO.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:398878 CAPLUS

DOCUMENT NUMBER: 129:146247

TITLE: Using Matrix-Assisted Laser Desorption Ionization Mass Spectrometry To Map the Quinol Binding Site of Cytochrome bo3 from Escherichia coli

AUTHOR(S): Tsatsos, Panagiota H.; Reynolds, Kate; Nickels, Elizabeth Furlong; He, Da-Yan; Yu, Chang-An; Gennis, Robert B.

CORPORATE SOURCE: School of Chemical Sciences, University of Illinois, Urbana, IL, 61801, USA

SOURCE: Biochemistry (1998), 37(28), 9884-9888
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cytochrome bo3 ubiquinol oxidase contains at least one and possibly two binding sites for ubiquinol/ubiquinone. Previous studies used the photoreactive affinity label 3-[3H]azido-2-methyl-5-methoxy-6-geranyl-1,4-benzoquinone (azido-Q), a substrate analog, to demonstrate that subunit II contributes to at least one of the quinol binding sites. In the current work, mass spectroscopy is used to identify a peptide within subunit II that is photolabeled by the azido-Q. Purified cytochrome bo3 was photolabeled as previously described using azido-Q that was not tritiated (i.e., not radiolabeled). Subunit II was then isolated from an SDS-PAGE gel and proteolyzed in situ with trypsin. The resulting peptides were eluted from the gel and then identified using matrix-assisted laser desorption ionization mass spectrometry. The resulting mass spectrum was compared to that obtained by anal. of subunit II that had not been exposed to the photolabel. Using the amino acid sequence, each peak in the mass spectrum of the unlabeled subunit II could be assigned to an expected trypsin fragment. Two addnl. peaks were observed in the mass spectrum of the photolabeled subunit with m/z 1931.9 and 2287.7. Subtraction of the mass of azido-Q from the peak at m/z 1931.9 results in a mass equivalent to that of a peptide consisting of amino acids 165-178. The assignment of the peak at m/z 2287.7 cannot be made unequivocally and may correspond either to the covalent attachment of azido-Q to peptide 254-270 or to a peptide resulting from incomplete proteolysis. The labeled peptide, 165-178, is within the water-soluble domain of subunit II, whose X-ray structure is known. This peptide is located near the site where CuA is located in the homologous cytochrome c oxidases and can be placed near the interface between subunits I and II.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:73769 CAPLUS

DOCUMENT NUMBER: 110:73769

TITLE: Peptides corresponding to antigenic and immunogenic determinants of major neutralizing proteins of rotaviruses and their diagnostic and therapeutic uses

INVENTOR(S): Sabara, Marta I.; Frenchick, Patrick J.; Potter, Andrew A.; Ijaz, Mohammad K.; Gilchrist, James E.
 PATENT ASSIGNEE(S): University of Saskatchewan, Can.
 SOURCE: Eur. Pat. Appl., 77 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 235391	A2	19870909	EP 1986-117981	19861223
EP 235391	A3	19880504		
EP 235391	B1	19920610		
R: BE, CH, DE, FR, GB, LI, NL, SE				
CA 1327096	A1	19940215	CA 1986-526116	19861223
AU 8666987	A1	19870702	AU 1986-66987	19861224
AU 600460	B2	19900816		
CN 86108975	A	19880106	CN 1986-108975	19861225
CN 1020857	B	19930526		
JP 63115825	A2	19880520	JP 1986-308945	19861226
US 6086880	A	20000711	US 1993-89397	19930707
PRIORITY APPLN. INFO.:			US 1985-813661	A 19851226
			US 1986-903325	A 19860903
			US 1988-241761	B1 19880907
			US 1990-552350	B2 19900712
			US 1990-626041	B2 19901210
			US 1991-661859	B1 19910227

AB Synthetic peptides corresponding to antigenic determinants of 3 major neutralizing proteins of bovine rotavirus [the 41,000-dalton (41K) neutralizing glycoprotein VP7, the 45K nucleocapsid protein VP6, and the 84K neutralizing glycoprotein VP3] are disclosed. These peptides are useful in stimulating immunity and interfering with viral infectivity and can be used as vaccines and in other ways for treatment, prevention, or diagnosis of rotavirus infections in birds and animals including man. The 14K peptide (165-295) of VP7 of bovine rotavirus C486, subclone 13, prepared by electrophoresis and enzymic digestion of the virus, was conjugated to bovine serum albumin via glutaraldehyde and used to immunize mice. A similar and significant immune response was seen to VP7, the 14K peptide, and the conjugate.

=> D L5 IBIB ABS 1-8

L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1324290 CAPLUS

DOCUMENT NUMBER: 144:106196

TITLE: HLA-A*0201, HLA-A*1101, and HLA-B*0702 Transgenic Mice Recognize Numerous Poxvirus Determinants from a Wide Variety of Viral Gene Products. [Erratum to document cited in CA143:365211]

AUTHOR(S): Pasquetto, Valerie; Bue, Huynh-Hoa; Giannino, Rielle; Banh, Cindy; Mirza, Fareed; Sidney, John; Oseroff, Carla; Tschärke, David C.; Irvine, Kari; Bennink, Jack R.; Peters, Bjoern; Southwood, Scott; Cerundolo, Vincenzo; Grey, Howard; Yewdell, Jonathan W.; Sette, Alessandro

CORPORATE SOURCE: La Jolla Institute for Allergy and Immunology, San Diego, CA, 92109, USA

SOURCE: Journal of Immunology (2005), 175(12), 8440

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cindy Banh, affiliated with the La Jolla Institute for Allergy and Immunol., San Diego, California, is added as the fourth author.

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1290557 CAPLUS
DOCUMENT NUMBER: 144:49767
TITLE: Immunodominance of Poxviral-Specific CTL in a Human
Trial of Recombinant-Modified Vaccinia Ankara
AUTHOR(S): Smith, Caroline L.; Mirza, Fareed; Pasquetto, Valerie;
Tscharke, David C.; Palmowski, Michael J.; Dunbar, P.
Rod; Sette, Alessandro; Harris, Adrian L.; Cerundolo,
Vincenzo
CORPORATE SOURCE: Tumour Immunology Unit, Weatherall Institute of
Molecular Medicine, Oxford University, Oxford, UK
SOURCE: Journal of Immunology (2005), 175(12), 8431-8437
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Many recombinant poxviral vaccines are currently in clin. trials for cancer and infectious diseases. However, these agents have failed to generate T cell responses specific for recombinant gene products at levels comparable with T cell responses associated with natural viral infections. The recent identification of vaccinia-encoded CTL epitopes, including a new epitope described in this study, allows the simultaneous comparison of CTL responses specific for poxviral and recombinant epitopes. The authors performed detailed kinetic analyses of CTL responses in **HLA-A*0201** patients receiving repeated injections of recombinant modified vaccinia Ankara encoding a string of melanoma tumor Ag epitopes. The vaccine-driven CTL hierarchy was dominated by modified vaccinia Ankara epitope-specific responses, even in patients who had not received previous **smallpox** vaccination. The only recombinant epitope that was able to impact on the CTL hierarchy was the melan-A26-35 analog epitope, whereas responses specific for the weaker affinity epitope NY-ESO-1157-165 failed to be expanded above the level detected in pre-vaccination samples. The results demonstrate that immunodominant vaccinia-specific CTL responses limit the effectiveness of poxviruses in recombinant vaccination strategies and that more powerful priming strategies are required to overcome immunodominance of poxvirus-specific T cell responses.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1144550 CAPLUS
DOCUMENT NUMBER: 144:49757
TITLE: Accurate Mass Precursor Ion Data and Tandem Mass Spectrometry Identify a Class I Human Leukocyte Antigen A*0201-Presented Peptide Originating from Vaccinia Virus
AUTHOR(S): Johnson, Kenneth L.; Ovsyannikova, Inna G.; Madden, Benjamin J.; Poland, Gregory A.; Muddiman, David C.
CORPORATE SOURCE: The W. M. Keck FT-ICR Mass Spectrometry Laboratory, and Mayo Proteomics Research Center, Mayo Clinic College of Medicine, Rochester, MN, USA
SOURCE: Journal of the American Society for Mass Spectrometry (2005), 16(11), 1812-1817
CODEN: JAMSEF; ISSN: 1044-0305
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have used accurate mass precursor ion data generated on a hybrid linear-ion trap-Fourier transform ion cyclotron resonance mass spectrometer to augment tandem mass spectrometry (MS/MS) data generated on two different instrument types. Results from these expts. have allowed the authors for the first time to identify a naturally processed peptide presented by a class I human leukocyte antigen allele (**HLA-A*0201**) that was isolated from B cells infected by live vaccinia, the viral agent of the **smallpox** vaccine. The accurate mass data, in conjunction with MS/MS data, was able to identify the sequence IVIEAIHTV (aa 187-195) from the protein thymidylate kinase of vaccinia, distinguishing it from a similar sequence IVLEAIAEH: a

"self-peptide" from the human protein phospholipase C β 3. Accurate mass data for the doubly charged species from the naturally processed and presented peptide was 497.8006, which was within 0.8 ppm of the calculated m/z of 497.8002, while being -37.3 ppm from the calculated m/z (497.7820) of the second-ranked peptide sequence IVLEAIAEH. Accurate mass data ranged from less than 0.1 to 1.2 ppm for other peptides identified in this sample. A BLAST search shows this sequence, IVIEAIHTV, is conserved in the same protein of a number of other orthopoxviruses, including the variola (**smallpox**) virus. Addnl., accurate mass data were able to uncover a false pos. search result that was not distinguished by scoring of the match to the MS/MS data.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1086416 CAPLUS

DOCUMENT NUMBER: 143:365211

TITLE: **HLA-A*0201**, HLA-A*1101,
and HLA-B*0702 Transgenic Mice Recognize Numerous
Poxvirus Determinants from a Wide Variety of Viral
Gene Products

AUTHOR(S): Pasquetto, Valerie; Bui, Huynh-Hoa; Giannino, Rielle;
Mirza, Fareed; Sidney, John; Oseroff, Carla; Tschärke,
David C.; Irvine, Kari; Bennink, Jack R.; Peters,
Bjoern; Southwood, Scott; Cerundolo, Vincenzo; Grey,
Howard; Yewdell, Jonathan W.; Sette, Alessandro

CORPORATE SOURCE: La Jolla Institute for Allergy and Immunology, San
Diego, CA, 92109, USA

SOURCE: Journal of Immunology (2005), 175(8), 5504-5515

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In virus models explored in detail in mice, CTL typically focus on a few immunodominant determinants. In this study the authors use a multipronged approach to understand the diversity of CTL responses to vaccinia virus, a prototypic poxvirus with a genome .apprx.20-fold larger than that of the model RNA viruses typically studied in mice. Based on predictive computational algorithms for peptide binding to HLA supertypes, the authors synthesized a panel of 2889 peptides to begin to create an immunomic map of human CTL responses to poxviruses. Using this panel in conjunction with CTLs from vaccinia virus-infected HLA transgenic mice, the authors identified 14 **HLA-A*0201**-, 4 **HLA-A*1101**-, and 3 **HLA-B*0702**-restricted CD8+ T cell determinants distributed over 20 distinct proteins. These peptides were capable of binding one or multiple A2, A3, and B7 supertype mols. with affinities typical of viral determinants. Surprisingly, many of the viral proteins recognized are predicted to be late gene products, in addition to the early intermediate gene products expected. Nearly all of the determinants identified have identical counterparts encoded by modified vaccinia virus Ankara as well as variola virus, the agent of **smallpox**. These findings have implications for the design of new **smallpox** vaccines and the understanding of immune responses to large DNA viruses in general.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1120687 CAPLUS

DOCUMENT NUMBER: 142:153764

TITLE: Recombinant modified vaccinia ankara primes
functionally activated CTL specific for a melanoma
tumor antigen epitope in melanoma patients with a high
risk of disease recurrence

AUTHOR(S): Smith, Caroline L.; Dunbar, P. Rod; Mirza, Fareed;
Palmowski, Michael J.; Shepherd, Dawn; Gilbert, Sarah
C.; Coulie, Pierre; Schneider, Joerg; Hoffman, Eric;
Hawkins, Robert; Harris, Adrian L.; Cerundolo,
Vincenzo

CORPORATE SOURCE: Tumour Immunology Unit, Weatherall Institute of Molecular Medicine, Nuffield Department of Clinical Medicine, Oxford University, Oxford, UK

SOURCE: International Journal of Cancer (2005), 113(2), 259-266
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB. Recombinant plasmid DNA and attenuated poxviruses are under development as cancer and infectious disease vaccines. We present the results of a phase I clin. trial of recombinant plasmid DNA and modified vaccinia Ankara (MVA), both encoding 7 melanoma tumor antigen cytotoxic T lymphocyte (CTL) epitopes. **HLA-A*0201**-pos. patients with surgically treated melanoma received either a "prime-boost" DNA/MVA or a homologous MVA-only regimen. Ex vivo tetramer anal., performed at multiple time points, provided detailed kinetics of vaccine-driven CTL responses specific for the high-affinity melan-A26-35 analog epitope. Melan-A26-35-specific CTL were generated in 2/6 patients who received DNA/MVA (detectable only after the first MVA injection) and 4/7 patients who received MVA only. Ex vivo ELISPOT anal. and in vitro proliferation assays confirmed the effector function of these CTL. Responses were seen in **smallpox** vaccinated as well as vaccinia-naïve patients, as defined by anti-vaccinia antibody responses demonstrated by ELISA assay. The observations that 1) CTL responses were generated to only 1 of the recombinant epitopes and 2) that the magnitude of these responses (0.029-0.19% CD8+ T cells) was below the levels usually seen in acute viral infections suggest that to ensure high nos. of CTL specific for multiple recombinant epitopes, a deeper understanding of the interplay between CTL responses specific for the viral vector and recombinant epitopes is required.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:292135 CAPLUS

DOCUMENT NUMBER: 138:383748

TITLE: Quantitation of CD8+ T cell responses to newly identified **HLA-A*0201**-restricted T cell epitopes conserved among vaccinia and variola (**smallpox**) viruses

AUTHOR(S): Terajima, Masanori; Cruz, John; Raines, Gregory; Kilpatrick, Elizabeth D.; Kennedy, Jeffrey S.; Rothman, Alan L.; Ennis, Francis A.

CORPORATE SOURCE: Center for Infectious Disease and Vaccine Research, University of Massachusetts Medical School, Worcester, MA, 01655, USA

SOURCE: Journal of Experimental Medicine (2003), 197(7), 927-932
CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Immunization with vaccinia virus resulted in long-lasting protection against **smallpox** and was the approach used to eliminate natural **smallpox** infections worldwide. Due to the concern about the potential use of **smallpox** virus as a bioweapon, **smallpox** vaccination is currently being reintroduced. Severe complications from vaccination were associated with congenital or acquired T cell deficiencies, but not with congenital agammaglobulinemia, suggesting the importance of T cell immunity in recovery from infection. In this report, the authors identified two CD8+ T cell epitopes restricted by the most common human major histocompatibility complex (MHC) class I allele, **HLA-A*0201**. Both epitopes are highly conserved in vaccinia and variola viruses. The frequency of vaccinia-specific CD8+ T cell responses to these epitopes measured by interferon (IFN)- γ enzyme-linked immunospot (ELISPOT) assay and HLA/peptide tetramer staining peaked 2 wk after primary immunization and then declined, but were still detectable 1 to 3 yr after primary immunization. 2 Wk after immunization,

IFN- γ -producing cells specific to these two epitopes were 14% of total vaccinia virus-specific IFN- γ -producing cells in one donor, 35% in the second donor, and 6% in the third donor. This information will be useful for studies of human T cell memory and for the design and analyses of the immunogenicity of expt1. vaccinia vaccines.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:43741 CAPLUS

DOCUMENT NUMBER: 138:151852

TITLE: Identification of vaccinia virus epitope-specific
HLA-A*0201-restricted T
cells and comparative analysis of **smallpox**
vaccines

AUTHOR(S): Drexler, Ingo; Staib, Caroline; Kastenmuller,
Wolfgang; Stevanovic, Stefan; Schmidt, Burkhard;
Lemonnier, Francois A.; Rammensee, Hans-Georg; Busch,
Dirk H.; Bernhard, Helga; Erfle, Volker; Sutter, Gerd
CORPORATE SOURCE: GSF-Institut fur Molekulare Virologie, Institut fur
Virologie, Technische Universitat Munchen (TUM),
Munchen, 81675, Germany

SOURCE: Proceedings of the National Academy of Sciences of the
United States of America (2003), 100(1), 217-222
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Despite worldwide eradication of naturally occurring variola virus, **smallpox** remains a potential threat to both civilian and military populations. New, safe **smallpox** vaccines are being developed, and there is an urgent need for methods to evaluate vaccine efficacy after immunization. Here we report the identification of an immunodominant **HLA-A*0201**-restricted epitope that is recognized by cytotoxic CD8+ T cells and conserved among Orthopoxvirus species including variola virus. This finding has permitted anal. and monitoring of epitope-specific T cell responses after immunization and demonstration of the identified T cell specificity in an A*0201-pos. human donor. Vaccination of transgenic mice allowed us to compare the immunogenicity of several vaccinia viruses including highly attenuated, replication-deficient modified vaccinia virus Ankara (MVA). MVA vaccines elicited levels of CD8+ T cell responses that were comparable to those induced by the replication-competent vaccinia virus strains. Finally, we demonstrate that MVA vaccination is fully protective against a lethal respiratory challenge with virulent vaccinia virus strain Western Reserve. Our data provide a basis to rationally estimate immunogenicity of safe, second-generation poxvirus vaccines and suggest that MVA may be a suitable candidate.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:671773 CAPLUS

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TITLE: Modified vaccinia virus ankara for delivery of human
tyrosinase as melanoma-associated antigen: induction
of tyrosinase- and melanoma-specific human leukocyte
antigen A*0201-restricted cytotoxic T cells in vitro
and in vivo

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AB . Vaccination with tumor-associated antigens is a promising approach for cancer immunotherapy. Because the majority of these antigens are normal self antigens, they may require suitable delivery systems to promote their immunogenicity. A recombinant vector based on the modified vaccinia virus Ankara (MVA) was used for expression of human tyrosinase, a melanoma-specific differentiation antigen, and evaluated for its efficacy as an antitumor vaccine. Stable recombinant viruses (MVA-hTyr) were constructed that have deleted the selection marker lacZ and efficiently expressed human tyrosinase in primary human cells and cell lines. Tyrosinase-specific human CTLs were activated in vitro by MVA-hTyr-infected, **HLA-A*0201**-pos. human dendritic cells. Importantly, an efficient tyrosinase- and melanoma-specific CTL response was induced in vitro using MVA-hTyr-infected autologous dendritic cells as activators for peripheral blood mononuclear cells derived from **HLA-A*0201**-pos. melanoma patients despite prior vaccination against **smallpox**. Immunization of **HLA-A*0201**/Kb transgenic mice with MVA-hTyr induced A*0201-restricted CTLs specific for the human tyrosinase-derived peptide epitope 369-377. These in vivo primed CTLs were of sufficiently high avidity to recognize and lyse human melanoma cells, which present the endogenously processed tyrosinase peptide in the context of A*0201. Tyrosinase-specific CTL responses were significantly augmented by repeated vaccination with MVA-hTyr. These findings demonstrate that HLA-restricted CTLs specific for human tumor-associated antigens can be efficiently generated by immunization with recombinant MVA vaccines. The results are an essential basis for MVA-based vaccination trials in cancer patients.

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